Constituents from Formosan Peucedanum japonicum

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Abstract

Three new khellactone esters, (-)-trans-3'-acetyl-4'-senecioyl-khellactone, (±)-cis-4'-tigloylkhellactone, (+)-trans-4'-tigloylkhel-lactone, together with 14 known coumarins, isoimperatorin, psoralen, bergapten, xanthotoxol, cnidilin, (-)-selinidin, (-)-deltoin, (+)-pteryxin, (+)-peucedanocoumarin III , xanthotoxin, imperatorin, (+)-marmesin, (+)-oxypeucedanin hydrate, (+)-peucedanol and three chromones, eugenin, (-)-hamaudol, (+)-visamminol, have been isolated from the root of Formosan Peucedanum japonicum (Umbelliferae). The structures of the new compounds were elucidated by spectral data.

Key Word Index : Peucedanum japonicum; Umbelliferae; coumarin; khellactone; chromone.

Introduction

Peucedanum japonicum Thunb. (Umbelliferae) is a perennial herb distributed in Japan, Philipines, mainland China and Taiwan. In Taiwan, it is plentiful in the coastal area of northern part and Lanyu Island [1]. The root was used as a folk medicine in the treatment of cold [2]. The chemical constituents of this plant were studied to some extent [3-12] and the khellactone coumarins were shown as the characteristic components. Examination of CHCl3-soluble part of the MeOH ext. of the root of this plant has led to the isolation of three new khellactones esters and seventeen known compounds as isoimperatorin [13], psoralen [13], bergapten [3], xanthotoxol [13], eugenin [14], cnidilin [15], (-)-selinidin [16], (-)-deltoin [17], (+)-pteryxin [18, 19], (+)-peucedanocoumarin III [18], xanthotoxin [13], imperatorin [17], (-)-hamaudol [13], (+)-visamminol [13], (+)-marmesin [20], (+)-oxypeucedanin hydrate [13] and (+)-peucedanol [17]. We report herein the structural elucidation of these new compounds.

Materials and Methods

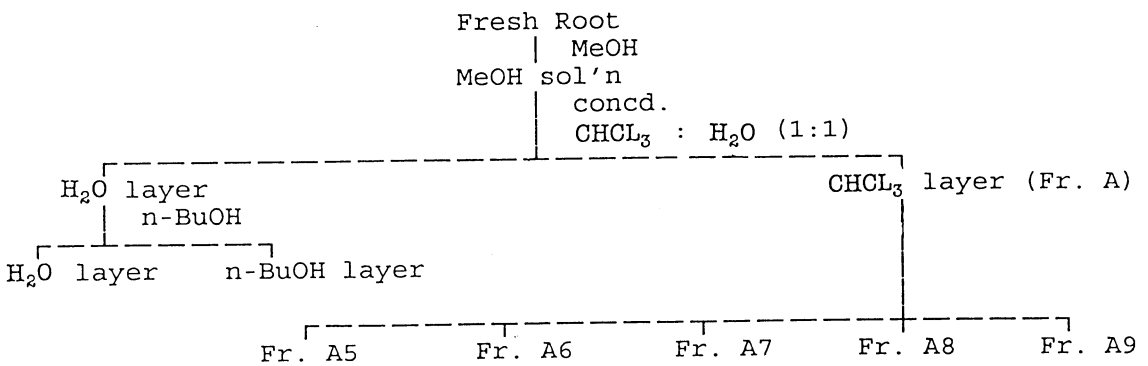
General Experimental Procedures

MPS: uncorr. ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50 MHz): $CDCl_3$ with TMS as int. standard; MS: 70ev; cc: silica gel 60 (70-230 mesh and 230-400 mesh) (Merck); TLC and prep. TLC: silica gel 60 GF 254 (Merck).

Plant Material

P. japonicum was collected at Lanyu Island, Taitung Hsien, Taiwan, in July 1991. The voucher specimen is deposited in the Herbarium of School of Pharmacy, Kaohsiung Medical College, Taiwan, Republic of China.

Extraction and separation



Results and Discussion

(-)-trans-3'-Acetyl-4'-senecioylkhellactone was isolated as an oil. The IR spectrum showed a ketone absorption at 1740 cm^{-1}. The UV spectrum showed maximal absorptions at 204, 220sh, 255sh, 295sh, 323 nm and indicated the presence of a 7-oxygenated coumarin moiety. In the 1H-NMR spectrum, the presence of two pairs of doublets [δ 6.23, 7.60 (each 1H, d, J=9.5 Hz, H-3 and H-4), δ 7.37, 6.82 (each 1H, d, J=8.6 Hz, H-5 and H-6)], two methyl singlets [δ 1.38, 1.46 (each 3H, s)], doublets of two vicinal methine protons [δ 5.31, 6.20 (each 1H, d, J=3.4 Hz, H-3' and H-4')], one acetoxy singlet [δ 2.10 (3H, s)] and one senecioyloxy group [δ 5.62 (1H, m, H-2"), δ 2.24 (3H, d, J= 1.2 Hz, 5"-Me), δ 1.89 (3H, d, J=1.1 Hz, 4"-Me)], suggested a khellactone diester as acetyl-senecioylkhellactone. The EI mass spectrum showed $[M]^+$ at m/z 386, the important ion fragments at m/z 326 $[M-60]^+$, 311 $[M-75]^+$, 287 $[M-99]^+$,

and informed of the location of these two acyl grs., an acetoxy gr. at C-3' and a senecioyloxy gr. at C-4', respectively [21]. The relative configuration of this khellactone ester indicated as trans-form due to the coupling constant $J_{3',4'}$ as 3.4 Hz [22] and was further evidenced by the chemical shift difference of gem-dimethyl signals in 13C- NMR as 0.12 ppm, lower than 2 ppm [23]. From above data and $[\alpha]_D^{25}$: -7.0° ($CHCl_3$, c 0.14), the new compound was elucidated as (-)-trans-3'-acetyl-4'-senecioylkhellactone.

(±)-cis-4'-Tigloylkhellactone was obtained as needles and the molecular formula, $C_{19}H_{20}O_6$, determined by EI ($[M]^+$, m/z 344) and HR mass spectrometry. The UV absorptions were very similar to those of (-)-trans-3'-acetyl-4'-senecioylkhellactone- and a 7-oxygenated coumarin moiety was suggested. The IR spectrum indicated the presence of a ketone group (1720 cm^{-1}) and the hydroxy group (3490 cm^{-1}). In the ^1H-NMR spectrum, the existence of two pairs of doublets [δ 6.23, 7.61 (each 1H, d, J= 9.5 Hz, H-3 and H-4), δ 7.37, 6.81 (each 1H, d, J=8.6 Hz, H-5 and H-6)], a closer two methyl singlets [δ 1.44, 1.48 (each 3H, s)], two vicinal methine protons [δ 4.07 (1H, dd, J=4.7, 2.6 Hz, H-3'), δ 6.47 (1H, d, J=4.7, H-4')], one hydroxy group [δ 2.98 (1H, br.d, J=2.6 Hz, 3'-OH)] and a tigloyloxy group [δ 6.90 (1H, qq, J=7.1, 1.4 Hz, H-3"), δ 1.86 (3H, m, 5"-Me), δ 1.79 (dq, J=7.1, 1.3 Hz, 4"-Me)], a 4'-tigloyl-khellactone was suggested. The relative configuration of (±)-cis-4'-tigloylkhellactone was determined as cis- form due to the coupling constant $J_{3',4'}$ as 4.7 Hz [21], the dihydropropane gem-dimethyl signals appeared as two singlets closer together [22, 24] in the 1H-NMR spectrum and the chemical shifts of gem-dimethyl signals with 4.78 ppm difference in the ^{13}C-NMR spectrum was larger than 2 ppm in trans- form [23]. With $[\alpha]_D^{24}$: ± 0.0° (CHC_{13}, c 0.11), the sturcture of new compound thus was elucidated as (±)-cis-4'-tigloylkhellactone.

(+)-trans-4'-Tigloylkhellactone was isolated as prisms and the molecular formula was established as $C_{19}H_{20}O_6$ by EI and HR mass spectrometry ($[M^+]$, m/z 344). The IR spectrum indicated the presence of a ketone group (1715 cm^{-1}) and the hydroxy group (3425 cm^{-1}). Inspection of 1H-NMR spectrum of (±)-cis-4'-tigloylkhellactone led to a coumarin of 4'-tigloylkhellactone; angular dihydropyranocoumarin moiety [δ 6.24, 7.62 (each 1H, d, J=9.5 Hz, H-3 and H-4), δ 7.37, 6.83 (each 1H, d, J=8.6 Hz, H-5 and H-6), δ 1.40, 1.48 (each 3H, s, gem-Me), δ 3.94 (1H, dd, J=4.8, 3.4 Hz, H-3'), δ 3.46 (1H, br.d, J=3.4 Hz, 3'-OH), δ 6.10 (1H, d, J=4.8 Hz, H-4')], tigloyloxy group [356.87 (1H, qq, J=7.1, 1.4 Hz, H-3"), δ 1.84 (3H, m, 5"-Me), δ 1.78 (3H, dq, J=7.1, 1.3 Hz, 4"-Me)]. The coupling constant $J_{3',4'}$ of (+)-trans-4'-tigloylkhellactone is 4.8 Hz and it is difficult to assign the relative cofiguration of (+)-trans-4'-tigloylkhellactone to be of cis- form again due to the aformentioned cis- khellactone ester with $J_{3',4'}$=4.7 Hz. After comparisons of chemical shifts of natural khellactone esters with having acyl group at C-4', we found the chemical shift of H-4' in trans- form is in higher field than that of H-4' in cis- form, and in case of khellactone esters, pair of configuration isomers show consistently ca. 0.3 ppm difference. This observation supported the relative configuration of (+)-trans-4'-tigloylkhellactone is trans-form

with H-4'(δ 6.10), due to the 0.37 ppm difference of chemical shift compared with H-4'(δ 6.47) of (±)-cis-4'-tigloylkhellactone with cis- form. The gem-methyl signals of ^{1}H-NMR of (+)-trans-4'-tigloylkhellactone showed two separate signals (δ 1.40 and δ 1.48) like other trans- khellactone coumarins. With [α]$_D^{26}$: +254.1° ($CHCl_3$, c 0.14), the new khellactone monoester of (±)-cis-4'-tigloylkhellactone was elucidated as (+)-trans-4'-tigloylkhellactone.

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References

1. Kao, M. T. (1993) Umbelliferae in Flora of Taiwan, Editorial Committe of the Flora of Taiwan, Taipei, 2nd Edi., Vol. III , p.1010.

2. Gan, W. S. (1965) Manual of Medicinal Plants in Taiwan, National Research Institute of Chinese Medicine, Taiwan, Vol. 3, p.675.

3. Yen, K. Y., Lai, H. M. and Chen, W. S. (1966) J. Taiwan Pharm. Assoc. 18, 75.

4. Hata, K., Kozawa, M., Ikeshiro, Y. and Yen, K. Y. (1968) Yakugaku Zasshi 88, 513.

5. Yamada, Y., Hsu, C. S., Iguchi, K.. Suzuki, M., Hsu, H. Y. and Chen, Y. P. (1974) Tetrahedron Lett. 29, 2513.

6. Shigematsu, N., Kouno, I., and Kawano, N. (1982) Yakugaku Zasshi 102, 392.

7. Cisowski, W.(1983) Pol. J. Chem. 57, 1283 [C.A. (1985) 102, 218357t.]

8. Duh, C. Y., Wang, S. K. and Wu, Y. C. (1991) Phytochemistry 30, 2812.

9. Duh, C. Y., Wang, S. K. and Wu, Y. C.(1992) Phytochemistry 31, 1829.

10. Jong, T. T., Hwang, H. C., Jean, M. Y., Wu, T. S. and Teng, C. M. (1992) J.Nat. Prod. 55, 1396.

11. Ikeshiro, Y., Mase, I. and Tomita, Y. (1992) Phytochemistry 31, 4303.

12. Ikeshiro, Y., Mase, I. and Tomita, Y. (1993) Phytochemistry 33, 1543.

13. Baba, K., Hata. K., Kimura, Y., Matsuyama, Y. and Kozawa, M. (1981) Chem. Pharm. Bull. 29, 2565.

14. Ali, A. A., Makboul, M. A., Attia, A. A. and Ali, D. T. (1990) Phyto-chemistry 29, 625.

15. Sasaki, H., Taguchi, H., Endo, T. and Yosioka, I. (1980) Chem. Pharm. Bull. 28, 1847.

16. Swager, T. M. and Cardellina II , J. H. (1985) Phytochemistry 24, 805.

17. Baba, K., Yoneda, Y., Kozawa, M., Fujita, E., Wang, N. H. and Yuan, C. Q. (1989) Shoyakugaku Zasshi 43, 216.

18. Takata, M., Shibata, S. and Okuyama, T. (1990) Planta Med. 56, 307.

19. Rao, G. X., Niu, F. D. and Sun, H. D. (1990) Acta Botanica Yunnanica, 12, 434.

20. Ishii, H., Hosoya, K., Ishikawa, T. and Haginiwa, T. (1974) Yaku-gaku Zasshi 94, 309.

21. Shaath, N. A., Soine, T. O. and Shipchandler, M. T. (1976) J. Pharm. Sci. 65, 1028.

22. Lemmich, J., Lemmich, E. and Nielsen, B. E. (1966) Acta Chem. Scan. 20, 2497.

23. Macias, F. A., Massanet, G. M. Rodriquez-Luis, F., Salv'a, J. and Fronczek, F. R. (1989) Magn. Reson. Chem. 27, 653.

24. Bellino, A., Venturella, P., Marino, M. L. Servettaz, O. and Venturella, G. (1986) Phytochemistry 25, 1195.

摘　要

對台灣產繖形科(Umbelliferae)植物牡丹防風(Peucedanum japonicum) 根部進行化學成分研究，由皮部之甲醇抽出液以CHCl3與H2O進行分配，所得之CHCl3層進行分離迄今得到14種已知香豆素類化合物：isoimperatorin, psoralen, bergapten, xanthotoxol, cnidilin, (-)-selinidin, (-)-deltoin, (+)-pteryxin, (+)-peucedanocoumarin III, xanthotoxin, imperatorin, (+)-marmesin, (+)-oxypeucedanin hydrate, (+)-peucedanol，3種chromone類化合物：eugenin, (-)-hamaudol, (+)-visamminol，及3種新khellactone esters化合物：(-)-trans-3'-acetyl-4'-senecioylkhellactone, (±)-cis-4'-tigloylkhellactone, (+)-trans-4'-tigloylkhellactone，這些化合物之結構皆以光譜數據而決定。